REMARKS

I. Status of the Claims

Prior to the Action, claims 5-9, 12-33, and 38 were pending, and have been examined. No claims have been cancelled. Claims 5, 33, and 38 have been amended. No new claims have been added.

Claims 5-9, 12-33, and 38 are therefore currently pending in the application.

II. Support for the Amendments to the Specification and Claims

Support for the amendments to the specification and claims can be found throughout the drawings, specification, and claims as originally filed.

Table 1 of the specification has been amended to correct clerical errors that have come to the attention of Applicants. Specific support for the amendment to Table 1 can be found in the specification as originally filed. Applicants hereby state that the errors appearing in Table 1 of the specification as originally filed occurred with no deceptive intent.

Specific support for the amendments to claim 5 can be found at least in part in paragraph 24 and Table 1 of the specification as originally filed.

Specific support for the amendments to claim 33 can be found at least in part in paragraph 24 and Table 1 of the specification as originally filed.

Specific support for the amendments to claim 38 can be found at least in part in paragraph 24 and Table 1 of the specification as originally filed.

It will be understood that no new matter is included in the amendments to the specification or the claims.

III. Table 1

It has come to Applicants' attention that certain information presented in Table 1 of the specification as originally filed is in error. Although these errors occurred without deceptive intent, and are not believed to impact the enablement of the presently claimed subject matter, or any other disclosed inventions, in an abundance of caution Applicants have amended the specification to correct Table 1, and provide below a corrected version of Table 1 for the convenience of the Examiner, and to avoid any confusion that the errors in Table 1 as originally filed might cause. Below is the corrected version of Table 1:

Table 1: Differentiation conditions for neuroprogenitor cells

Culture condition for differentiation			
Days 1-4	Days 4-7	Days 8-50	TH positive cells (%)
Neurobasal medium, FCS, B27, IL-1β Not sorted	Neurobasal medium, FCS, B27, Shh, FGF-8, IL-1β, db-cAMP, GDNF, BDNF	Neurobasal medium, FCS, B27, Shh, FGF-8, IL-1β, db-cAMP, GDNF, BDNF, TGF-β3, neurturin	42%
Neurobasal medium, FCS, B27, IL-1β	Neurobasal medium, FCS, B27, Shh, FGF-8, IL-1β, db-cAMP, GDNF, BDNF, ascorbic acid	Neurobasal medium, FCS, B27, Shh, FGF-8, IL-1β, db-cAMP, GDNF, BDNF, TGF-β3, neurturin ascorbic acid	55%
Neurobasal medium, FCS, B27, IL-1β	Neurobasal medium, FCS, B27, Shh, FGF-8, IL-1β, db-cAMP, GDNF, BDNF, N-acetyl cysteine	Neurobasal medium, FCS, B27, Shh, FGF-8, IL-1β, db-cAMP, GDNF, BDNF, TGF-β3, neurturin N-acetyl cysteine	65%
Neurobasal medium, FCS, B27	Neurobasal medium, FCS, B27	Neurobasal medium, FCS, B27	20%

IV. Rejection of Claims 5-9, 12-33, and 38 under 35 U.S.C. §103(a)

The Action rejects claims 5-9, 12-33, and 38 under 35 U.S.C. § 103(a), as allegedly being unpatentable over Rolletschek, *et al.* (*Mech. Dev.* **105**:93-104, 2001 ("Rolletschek")) and further in view of International Patent Application Publication No. WO 2001/88104, published November 22, 2001 ("Carpenter") and United States Patent Application Publication No. US 2002/0068045, published June 6, 2002 ("Reubinoff"). Applicants respectfully traverse.

The Action states that "one of skill in the art would have a reasonable expectation of success in achieving differentiation of dopaminergic and serotonergic neurons by selecting nestin and NCAM positive cells from a population of human pluripotent cells, as taught by Carpenter and Reubinoff, and cultivating the selected cells in the presence of TGF-β3 and interleukin-1β, as taught by Rolletschek, to arrive at the generic methods of the instant claims" (the Action bridging pages 3 and 4). While Applicants in no way agree with this statement, Applicants respectfully point out that claims 5, 33, and 38 have been amended to recite that the cells are cultivated in the presence of N-acetyl cysteine, which is neither taught nor suggested by the Rolletschek, Carpenter, or Reubinoff references. In fact, N-acetyl cysteine is not mentioned at all in the Rolletschek, Carpenter, or Reubinoff references, much less the claimed combination of N-acetyl cysteine and TGF-β3 or interleukin-1β or both (therefore, Applicants do not believe it necessary to provide a lengthy discussion of the additional numerous shortcomings of these three references with respect to the pending claims). Since the Rolletschek, Carpenter, and Reubinoff references, alone or in any combination, do not teach or suggest the presently claimed subject matter, the rejection of claims 5-9, 12-33, and 38 under 35 U.S.C. § 103(a) over the Rolletschek, Carpenter, and Reubinoff references has been rendered moot.

Applicants therefore respectfully request that the rejection of claims 5-9, 12-33, and 38 under 35 U.S.C. § 103(a) be withdrawn.

V. Rejection of Claims 5-9, 12-33, and 38 under 35 U.S.C. §112, First Paragraph

The Action next rejects claims 5-9, 12-33, and 38 under 35 U.S.C. § 112, first paragraph, as allegedly not enabled for the full scope of the claims. Applicants respectfully traverse.

The Action states that "the specification, while being enabling for a method of generating a differentiated neural cell population from primate pluripotent stem cells wherein the differentiated neural cell population comprises at least about 60% dopaminergic neurons or at least about 30% serotonergic neurons, comprising the steps (a) expanding a culture of primate pluripotent stem cells; (b) forming embryoid bodies and selecting for neuroprogenitor cells that are positive for nestin by culturing the pluripotent stem cells in serum-free medium comprising insulin, sodium selenite, transferring, and fibronectin; (c) sorting the nestin-positive neuroprogenitor cells for enrichment of NCAM-positive cells; (d) differentiating the nestin-positive, NCAM-positive cells by culturing the cells in a differentiation media which comprises TGF-β3 or interleukin-1β, or both, does not reasonably provide enablement for any method that omits the steps of embryoid body formation or culturing the pluripotent stem cells in serum-free medium comprising insulin, sodium selenite, transferring, and fibronectin" (the Action bridging pages 4 and 5). By attempting to limit the claims only to a preferred embodiment, Applicants maintain that the Examiner appears to be applying an improper standard for compliance with the enablement requirement.

As set forth in the Manual of Patent Examining Procedure ("the MPEP"), Section 2164.01(b), "(a)s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied," *citing In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Furthermore, as set forth in the MPEP, Section 2164.01, all that is required for compliance with the enablement requirement is for the specification to teach "any person skilled in the art [to] make and use the invention without undue experimentation" *citing In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), and *United States v. Telectronics, Inc.*,857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). In addition, the Examiner admits that "(t)he instant specification does indeed teach a method that will yield a differentiated neuronal cell population comprising about 60% dopaminergic neurons or about 30% serotonergic neurons" (the Action at page 8). Since the skilled artisan, based on all of the teachings of the present specification, would clearly understand how to produce the claimed differentiated neural cell population comprising at least about 60% dopaminergic neurons or at least about 30% serotonergic neurons, the presently claimed subject matter complies with the enablement requirement.

The Action states that the present claims do not comply with the enablement requirement because "(d)ifferentiation without embryoid body formation, in the presence of serum, or in the absence of any component of ITFSn medium was not tested" (the Action at page 9). Applicants respectfully point out that compliance with the first paragraph of 35 U.S.C. § 112 does not require that each and every embodiment of the invention be demonstrated by actual working examples (*In re Gay*, 309 F.2d 768, 135 USPQ 311 (CCPA 1962)). The specification "need

describe the invention only in such detail as to enable a person skilled in the most relevant art to make and use it" (*In re Naquin*, 398 F.2d 863, 866, 158 USPQ 317, 319 (CCPA 1968)). Applicants stress that enablement must be analyzed not in a vacuum, but "as it would be interpreted by one possessing the ordinary level of skill in the pertinent art" (*In re Moore*, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (CCPA 1971)). Since the data presented in the specification shows production of the claimed differentiated neural cell population comprising at least about 60% dopaminergic neurons or at least about 30% serotonergic neurons, the present claims clearly meet the enablement requirement of the first paragraph of 35 U.S.C. § 112.

The Action also argues that the present claims fail to comply with the enablement requirement because "the instant claims recite method steps that are known in the art" (the Action at page 6), and that "(t)he guidance provided by the prior art is so thorough that claims that merely recite expansion of stem cells, selection of cells that are positive for nestin and NCAM, followed by differentiation in TGF-3β or interleukin-1β have been rejected for being obvious" (the Action at page 8). Applicants respectfully point out that the above statements essentially admit that the pending claims are enabled, and that this argument is simply a reiteration of the obviousness rejection previously set forth in the Action. As already detailed in Section IV, above, since the art cited in the rejection of the claims as obvious makes no mention whatsoever of N-acetyl cysteine, let alone teaches or suggests the use of N-acetyl cysteine, the rejections of the claims "for being obvious" has been overcome. In addition, this argument does not support the position of the Examiner that the pending claims fail to comply with the enablement requirement.

It also appears that the Examiner is requiring that the exact conditions from a preferred embodiment disclosed in the specification as originally filed be incorporated into the pending claims in order to comply with the enablement requirement. It has been well established by the Federal Circuit, however, that the specification teaches and enables, not the claims: "Specifications teach. Claims claim." (*SRI Int'l. v. Matsushita Elec. Corp. of Amer.*, 775 F.2d 1107, 1121, n.14 (Fed. Cir. 1985). Applicants are not required to test every possible value of each of the recited steps to enable the present claims, and one of skill in the art would clearly regard the claimed subject matter as enabled based on the present disclosure. Therefore, this argument in support of the enablement rejection is without merit, and should be withdrawn.

Since the specification as originally filed clearly enables the claimed methods of generating a differentiated neural cell population comprising at least about 60% dopaminergic neurons or at least about 30% serotonergic neurons, the presently claimed subject matter complies with all aspects of the enablement requirement. Applicants therefore respectfully request that the rejection of claims 5-9, 12-33, and 38 under 35 U.S.C. § 112, first paragraph, be withdrawn.

VI. Conclusion

Applicants believe this Response to be fully responsive to all outstanding issues, and to place this application in condition for allowance. Reconsideration of the application and allowance of the pending claims is respectfully requested. If the Examiner has any questions or comments regarding any issue associated with this application, a telephone call to the undersigned representative at 512.542.8569 is welcome.

Respectfully submitted,

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